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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,123	02/10/2005	Jose Ignacio Andres-Gil	JANS-0084/JAB1747PCTUS	4854

45511 7590 10/11/2007

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EXAMINER	
LEESER, ERICH A	
ART UNIT	**PAPER NUMBER**
1624	

NOTIFICATION DATE	DELIVERY MODE
10/11/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@woodcock.com

Office Action Summary	Application No.	Applicant(s)	
	10/524,123	ANDRES-GIL ET AL.	
	Examiner	Art Unit	
	Erich A. Leeser	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7 and 12* is/are rejected.

7)☐ Claim(s) *2-5,8-11 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2-10-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

In correspondence dated September 13, 2007, Applicant elected with traverse Group I directed to compounds when Het is pyridinyl and the composition thereof.

Applicant argues that the compound cited by Examiner in the previous Office action possesses a corresponding "Het" being dihydrofuranyl and the closest option to find anticipation listed in the present invention is an unsaturated furanyl moiety. This argument is found to be persuasive and as such Examiner withdraws the Restriction Requirement.

Claims 1-5 and 7-13 are pending and under examination.

Priority

Acknowledgment is made that this application is a 371 of PCT/EP03/50377, filed on August 13, 2002 and which claims benefit of foreign priority of EPO 02078373.4, filed on August 15, 2002.

Information Disclosure Statement

The references cited in the IDS, dated February 10, 2005, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for a "prophylaxis" of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The only established prophylactics are vaccines not the fused heterocyclic isoxazoline derivative compounds such as are present here. In addition, it is presumed that a prophylaxis of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) As discussed above, a prophylaxis of diseases requires identifying those patients who will acquire the disease before infection occurs. This would require extensive and potentially open-ended clinical research on healthy subjects. 2) Applicants intend a prophylaxis of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders. 3) There is no working example of such a preventive procedure in man or animal in

the specification. 4) The claims rejected are drawn to clinical pharmaceutical medicine and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become infected before the fact. 6) The artisan using Applicants' invention would be a Board Certified physician with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2d 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent a disease or condition generally. 7) It is well-established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula (I).

The Examiner suggests deletion of the word "prophylaxis" from claim 12 to obviate this rejection.

Claims 7 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant

compounds to treat and/or "prophylaxis" of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders with a therapeutically-effective amount of a compound of Formula (I) or enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention:

The instant invention is drawn to compositions used to treat and/or "prophylaxis" of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders with a therapeutically-effective amount of a compound of Formula (I).

The state of the prior art:

The state of the prior art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on

its face. For example, "the key for the next generation of progress is to unravel the complex effects of activation/antagonism of the various postsynaptic 5-HT receptors and their significance, *if any*, in mediating the antidepressant response." (Emphasis added). Cryan, J., et al., *5-HT_{1A} and Beyond: The Role of Serotonin and its Receptors in Depression and the Antidepressant Response*, Hum. Psychopharmacol. Clin. Exp. 15, 113-135 (2000). This reference shows the speculative nature of the role of 5-HT receptors with the treatment of depression.

The predictability in the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the claimed invention is highly unpredictable since one skilled in the art would not necessarily recognize, with regards to therapeutic effects, whether or not the compounds of claim 1 would be useful to treat and/or "prophylaxis" of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders.

Amount of guidance/working examples:

Although Applicant includes various "Pharmacological examples" in the end of the specification, none of these definitively show that the instant compounds can reliably be used to treat and/or "prophylaxis" of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders with a therapeutically-effective amount of a compound of Formula (I).

The breadth of the claims:

The claim terms are not unduly broad.

The quantity of undue experimentation needed:

Since the guidance and teaching provided by the specification is insufficient to treat and/or "prophylaxis" of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders with a therapeutically-effective amount of a compound of Formula (I), one of ordinary skill in the art, even with a high level of skill, is unable to practice the invention as claimed without undue experimentation.

The level of the skill in the art:

The level of skill in the art is high. Due to the unpredictability in the pharmaceutical art; however, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases or diseases would benefit from this activity.

Taking all of the above factors into consideration, it is not seen how one of ordinary skill in the art would be able to use Applicant's invention to treat and/or "prophylaxis" of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders with a therapeutically-effective amount of a compound of Formula (I) without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The following apply. Any claim not specifically rejected is rejected if it is dependent on a rejected claim and shares the same indefiniteness.

(a) Claim 1 is indefinite because one skilled in the art would not necessarily know which bond pair or pairs (c,d), (d,e) or (e,f) would be appropriate based on the designation of "Het" (see the fifteen choices on the bottom of page 2). It is confusing if one, two or all three of them are applicable and if only one or two of them then which ones?

Claim Objections

Claims 2-5, 8-11 and 13 are objected to as being dependent upon rejected independent claim 1, but would be allowable if rewritten in independent form including all of the limitations of the base claims and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leeser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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